CATALYTIC ENANTIOSELECTIVE ALLYLIC OXIDATION

Rispens, Minze T.; Zondervan, Charon; Feringa, Bernard

Published in:
Tetrahedron-Asymmetry

DOI:
10.1016/0957-4166(95)00054-S

Publication date:
1995

Pergamon

Tetrahedron: Asymmetry Vol. 6, No. 3, pp. 661-664, 1995
Elsevier Science Ltd
Printed in Great Britain
0957-4166/95 $9.50+0.00

0957-4166(95)00054-2

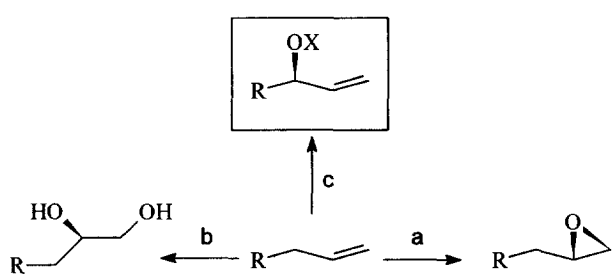
Catalytic Enantioselective Allylic Oxidation

Minze T. Rispens, Charon Zondervan and Ben L. Feringa*

Department of Organic and Molecular Inorganic Chemistry,
Groningen Centre for Catalysis and Synthesis,
University of Groningen,
Nijenborgh 4, 9747 AG Groningen,
The Netherlands.

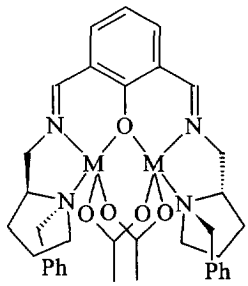
Abstract : Several chiral Cu(II)-complexes of cyclic amino acids catalyse the enantioselective allylic oxidation of cyclohexene to cyclohexenyl esters. Cyclohexenyl propionate was obtained in 86% yield with e.e.'s up to 61%.

Enantioselective oxygenation of olefins[1] and hydroxylation of alkanes[2] are particularly challenging goals in asymmetric synthesis. The efficient procedures for the epoxidation of allyl alcohols (Scheme 1, route a) and dihydroxylation of a wide range of olefins (Scheme 1, route b), developed by Sharpless and co-workers,[3,4] lead to virtually enantiomerically pure 1,2- and 1,3-functionalized products. Several catalytic asymmetric epoxidations of unfunctionalized olefins have been developed based on mononuclear metal complexes mimicking heme and non-heme oxygenases.[5] A major breakthrough in this respect was the discovery by Jacobsen and co-workers of the enantioselective epoxidation of alkenes by chiral manganese salen catalysts (Scheme 1, route a).[6]

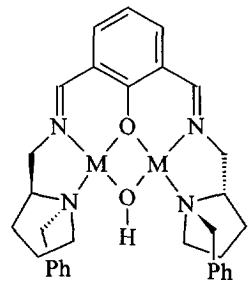


Scheme 1

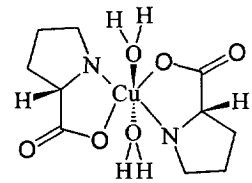
The asymmetric allylic oxidation (Scheme 1, route c) can be considered as an attractive alternative for direct functionalization of olefins exploiting the special nature of the allylic CH bond.[7] Following the early studies by Kharasch,[8] a number of copper complexes has been found to mediate the oxidation of olefins to allylic esters.[9,10] Furthermore, palladium(II) catalyzed allylic oxidation is well established[11] and recently a Pd(II)/benzoquinone system for allylic acetoxylation was reported.[12] Despite these findings and the synthetic potential[7] of the transformation depicted in scheme 1, route c, the asymmetric allylic oxidation has met little success so far.[13]



1 (M = Ni(II), Cu(II))



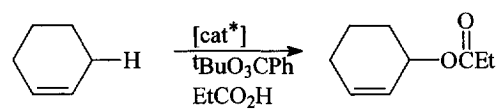
2 (M = Ni(II))



3

We wish to report a catalytic enantioselective allylic oxidation in the presence of propionic acid and peresters to yield allylpropionates. In preliminary experiments chiral dinuclear Ni(II) - and Cu(II) - complexes **1** and **2**, catalytically active in dehydrogenation[14] and epoxidation,[15] were used in the oxidation of cyclohexene and allylbenzene with *tert*-butylperoxy-acetate (or -propionate) but only low enantioselectivities (up to 10%) were reached.

Using cyclohexene as a model olefin it was subsequently found that enantioselectivities up to 35% could be reached under ambient conditions using Cu(II)-amino acid complexes and peracetates as oxidants in acetic acid. The conversions however were low. Much to our surprise both catalytic activity and enantioselectivity were greatly enhanced by adding 10 equiv. (with respect to Cu(II) catalyst) of copper bronze and employing a propionic acid/acetonitrile solvent mixture (Scheme 2).



Scheme 2 **4** **5**

In a typical reaction, using 0.5 mol% cupric acetate in the presence of 6 equiv. of (S)-proline as the ligand and *tert*-butylperoxybenzoate as the oxidant, cyclohexenyl propionate (**5**)[16] was obtained with 38% conversion and an enantiomeric excess of 51% after 16 hours at 0 °C. The influence of the variation of a number of reaction parameters is shown in Table 1. The use of Cu(II) triflate or Cu(I) cyanide lowers the enantioselectivity (entries 4 and 10) whereas the conversion is reduced employing Cu(I) triflate (entry 5). Without additional copper bronze only 5-9% conversion is reached albeit e.e.'s up to 57% are found. It should be noted that instead of copper the use of zinc results in 58% e.e. after 1 day at 20 °C, highlighting the role of the metal as reducing agent in the catalytic cycle (entry 9). The highest enantioselectivity (e.e. 61%) in the formation of **5**, at synthetically useful levels of conversion, was obtained using 20 equiv. of (S)-proline with respect to Cu(II) (10 mol% of chiral ligand) (entry 7). The yield of **5** could be further improved up to 70% when a larger amount of catalyst was employed (entry 8) without appreciable deterioration of the enantioselectivity. The results obtained so far suggest the involvement of a chiral copper-proline complex in the catalytic cycle. Structurally well defined bis-aquo-bis-(S)-prolinato-Cu(II)[17] (**3**) used in the presence of additional copper gave similar results compared to the *in situ* prepared copper proline catalyst (entry 2).

Table 1. Copper-(S)-proline catalysed cyclohexenyl ester formation.

entry	catalyst CuX_n(mol%)	Cu (mol%)	ligand (mol%)	temp (°C)	time (hours)	conversion[a] (%)	e.e.[b] (%)
1	$CuAc_2$ (0.5)	(5)[c]	proline (3)	0	16	71	35
2	$CuAc_2$ (0.5)	(5)	proline (3)	0	16	38	51
3	$CuAc_2$ (0.5)	(5)	proline (3)	0	60	74	41
4	$CuTf_2$ (0.4)	(5)	proline (3)	0	60	47	36
5	CuTf (0.3)[d]	(5)	proline (3)	0	60	20	44
6	$CuAc_2$ (0.5)	-	proline (3)	0	16	0	-
7	$CuAc_2$ (0.5)	(5)[e]	proline (10)	20	16	39	61
8	$CuAc_2$ (2.5)	(20)	proline (15)	20	16	70	57
9	$CuAc_2$ (0.5)	(5)[f]	proline (3)	20	16	14	58
10	CuCN (0.5)	(5)	proline (3)	0	16	25	15

[a] In all cases conversion to cyclohexenyl ester is denoted as determined by GC-analysis using n-dodecane as an internal standard. [b] Determined by chiral GC-analysis (HP5890A with a capillary column coated with CP cyclodextrin -B-2,3,6-M-19). [c] Acetic acid was used as solvent, product is cyclohexenyl acetate. [d] As its benzene complex. [e] 1.5 mL of 1,1-dimethylpropyl-peroxypivaloate was used. [f] 72 mg of zinc dust was used. When acyclic amino acids, chiral amines or amino alcohols were used as ligands under the standard reaction conditions (vide supra), allylic oxidation could be executed although e.e.'s of only 5-11% (18-48% yield) were found.

Next a variety of peresters was examined in the catalytic oxidation of cyclohexene using *in situ* prepared Cu(II)-(S)-proline complex (Table 2; entries 1-7). It is clearly seen that the yield of cyclohexenyl propionate strongly depends on the nature of the perester used whereas the enantioselectivity is much less influenced with e.e.'s in the range of 37 - 52%. In the series of peresters investigated so far 1,1-dimethylpropyl peroxypivaloate gives the highest selectivity.

Table 2. Variation of perester and amino acid ligand.

entry		temp (°C)	time (hours)	conversion (%)	e.e. (%)
	perester[a]				
1	*t*-Butylperoxyacetate	0	16	86	43
2	*t*-Butylperoxypropanoate	0	16	9	43
3	1,1-Dimethylpropylperoxypivaloate	0	16	6	52
4	*t*-Butylper-3-methyl-5-dimethylhexanoate	0	16	61	43
5	*t*-Butylperoxy-2,2-dimethylpropanoate	0	16	3	37
6	Di(*t*-butylperoxy)di-cyclohexanoate	0	16	23	37
7	*t*-Butylperoxybenzoate	0	16	43	45
	ligand[b]				
8	α-methyl-proline	0	16	11	20
9	α-benzyl-proline	0	16	37	26
10	N-benzyl-proline	0	16	18	7
11	azetidine-2-carboxylic acid	0	16	37	35
12	proline	0	16	50	42
13	pipecoline-2-carboxylic acid	0	16	7	8
14	indoline-2-carboxylic acid	20	16	34	7

[a] In entries 1-7 the same reaction conditions were used as described above using (S)-proline as chiral ligand. [b] In entries 8-14 the same reaction conditions were used as described above using *tert*-butylperoxybenzoate as oxidant.

In order to elucidate steric and electronic requirements of the chiral ligands employed, a number of cyclic amino acids was studied. (table 2; entries 8-14). Introduction of a methyl or benzyl substituent in the α-position of proline

lowered the e.e., whereas in the case of N-benzyl-(S)-proline, hardly any selectivity was observed. Variation of the ring size of the chiral ligand, i.e. (S)-proline, (S)-azetidine-2-carboxylic acid and (S)-pipecoline-2-carboxylic acid, resulted in a decrease in enantioselectivity. Finally, it should be noted that although the benzannelated proline analog (S)-indoline-2-carboxylic acid yields an active catalyst with Cu(II), the enantioselectivity is drastically reduced. In conclusion a catalytic system for the direct enantioselective allylic oxidation of cyclohexene has been found with attractive conversions and enantioselectivities, based on readily available amino acids ligands. Studies to improve the asymmetric induction and to extend the scope of the allylic oxidation towards other olefins are currently in progress.

Acknowledgement: *(S)-Azetidine-carboxylic acid was kindly provided by Prof. J. Martens (University of Oldenburg). We are greatfull to AKZO Chemicals, Deventer (Dr. A. Talma) for a gift of the peresters used in this study. This work was supported by the Netherlands Foundation of Chemical Research (NWO/SON)*

References and notes:

1. (a) *Metal-Catalyzed Oxidations of Organic Compounds*, Sheldon, R. A.; Kochi, J. K. Eds.; Academic Press: New York, 1981; (b) Jørgensen, K. A. *Chem. Rev.* **1989**, *89*, 431-458; (c) Mimoun, H. Metal Complexes in Oxidation. In *Comprehensive Coordination Chemistry*, Wilkinson, G.; Gillard, R. D.; McCleverty, J. A. Eds.; Pergamon: Oxford, **1987**, *6*, pp. 317-410.
2. *The Activation of Dioxygen and Homogeneous Catalytic Oxidation*, Barton, D. H. R.; Martell, A. E.; Sawyer, D. T. Eds.; Plenum: New York, 1993.
3. (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, pp. 5974-5976; (b) Johnson, R. A.; Sharpless, K. B. Catalytic Epoxidation of Allylic Alcohols. In *Catalytic Asymmetric Synthesis*, Ojima, I. Ed.; VCH: New York, 1993; pp. 103-158.
4. Johnson, R. A.; Sharpless, K. B. Catalytic Asymmetric Dihydroxylation. In *Catalytic Asymmetric Synthesis*, Ojima, I. Ed.; VCH: New York, 1993; pp. 227-272.
5. For a review, see: Jacobsen, E. N. Asymmetric Epoxidation of Unfunctionalized Olefins. In *Catalytic Asymmetric Synthesis*, Ojima, I. Ed.; VCH: New York, 1993, pp. 159-202.
6. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801-2803.
7. An attractive feature furthermore is that facile metal catalyzed replacement of the allylic acetate group by various nucleophiles can take place; Trost, B. M.; Verhoeven, T. R. Organopalladium Compounds in Organic Synthesis and in Catalysis. In *Comprehensive Organometallic Chemistry*, Wilkinson, G.; Stone, F. G. A.; Abel, E. W. Eds.; Pergamon: Oxford, **1982**, *8*, 799-938.
8. Kharasch, M. S.; Sosnovsky, G. *J. Am. Chem. Soc.* **1958**, *80*, 756.
9. (a) Denney, D. Z.; Appelbaum, A.; Denney, D. B. *J. Am. Chem. Soc.* **1962**, *84*, 4969-4971; (b) Walling, C.; Zavitsas, A. A. *J. Am. Chem. Soc.* **1963**, *85*, 2084-2090.
10. Beckwith, A. L. J.; Zavitsas, A. A. *J. Am. Chem. Soc.* **1986**, *108*, 8230-8234.
11. Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*, D. Reidel: Boston, 1980.
12. Åkermark, B.; Larsson, E. M.; Oslob, J. D. *J. Org. Chem.* **1994**, *59*, 5729-5733.
13. For a pertinent example, though with low optical activity, see: Patent 2,625,030, **1976**, Sumitomo Chemical Co.; C.A. **1977**, *86*, 120886.
14. Gelling, O. J.; Meetsma, A.; Feringa, B. L. *Inorg. Chem.* **1990**, *29*, 2816-2822.
15. Rispens, M. T.; Gelling. O. J.; de Vries, A. H. M.; Meetsma, A.; van Bolhuis, F. *J. Org. Chem.*, submitted.
16. Data of cyclohexenyl esters were in accordance with independently prepared samples.
17. The X-ray structure of complex **3** shows octahedral geometry with two water molecules in apical positions, see: Mathieson, A. McL.; Welsh, H. K. *Acta Cryst.* **1952**, *5*, 599-604.

(*Received in UK* 6 *January* 1995)